

**UNITED STATES DEPARTMENT OF COMMERCE****Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

8

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
-----------------	-------------	----------------------	---------------------

09/431,888 11/02/99 WISE

L 1064/44803

EXAMINER

HM12/1012
EVENSON MCKEOWN EDWARDS & LENAHAN PLLC
1200 G STREET N W
SUITE 700
WASHINGTON DC 20005

ANDRES, J

ART UNIT

PAPER NUMBER

1646

10

DATE MAILED:

10/12/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/431,888	WISE ET AL.
	Examiner Janet L Andres	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-52 is/are pending in the application.
 - 4a) Of the above claim(s) 8-52 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-7 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - a) All b) Some * c) None of the CERTIFIED copies of the priority documents have been:
 1. received.
 2. received in Application No. (Series Code / Serial Number) _____.
 3. received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
17) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____	20) <input type="checkbox"/> Other: _____

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Invention I, claims 1-7, in paper no. 9 is acknowledged. Claims 8-52 are withdrawn from consideration as being drawn to a non-elected invention.

Priority

2. Applicant's claim to priority based on provisional applications 60/106689, filed Nov. 2, 1998, and 60/106800, filed Nov. 3, 1998, is acknowledged.

Specification

3. The specification is objected to because the Brief Description of the Drawings on pages 27 and 28 does not include a reference to A and B of Figure 4.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for stimulating proliferation of endothelial cells with ORFV2-VEGF, does not reasonably provide enablement for stimulation of any other cell type or for stimulation by NZ10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or

absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman*, (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988). In the instant specification, applicant has provided objective evidence that ORFV2-VEGF can function as an endothelial cell mitogen. However, no guidance is present to indicate to one of skill in the art that ORFV2-VEGF could function to stimulate proliferation of mesodermal cells as instantly claimed. Since VEGF is known to function specifically as an endothelial cell growth factor (Thomas, J. Biol. Chem. Vol. 271, pp. 603-606, 1996), one of skill would not predict, without further guidance, that a VEGF analogue would function as a mesodermal cell mitogen. Applicant states that ORFV2-VEGF binds to VEGF receptor-2; this receptor is expressed on endothelial cells (Thomas, above, p. 603). Thus one of skill would not predict that a ligand for this receptor would have any effect on mesodermal cells. In addition, although applicant states that NZ10 is 87% homologous to ORFV2-VEGF, this homology is insufficient to imply a similar function or any function at all. Small changes may in fact result in loss of the ability to bind or activate a receptor. For example, addition of a single methionine to the chemokine RANTES converts it into an antagonist (Proudfoot et al., J. Biol. Chem. Vol 271, pp. 2599-2603, 1996). Since accurate predictions from mere sequence data are thus limited, the guidance in the instant specification is inadequate to indicate to one of skill that NZ10 would function as an agonist, rather than as an antagonist, of VEGF receptor-2. Thus without further direction, one of skill in the art would not be able to use NZ10 as a mitogen, or ORFV2-VEGF as a mesodermal cell mitogen, with a reasonable expectation of success. Further, activation of VEGF receptor-2 by ORFV2-VEGF appears to be

substantially less effective than activation by VEGF. There is no objective evidence to indicate that activation is "specific" for VEGF receptor-2, as claimed in claims 5 and 6; the evidence does not preclude the existence of other receptors through which ORFV2-VEGF might function. Thus one of skill would not predictably be able to use ORFV2-VEGF for "specific activation" of VEGF receptor-2 as claimed.

Since is therefore not predictable that the invention would function as claimed, it would require undue experimentation for one of skill in the art to practice the invention commensurate with the scope of the instant claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to a method comprising exposing cells to an effective "endothelial or mesodermal cell proliferation stimulating amount". Applicant has not indicated what such an amount might be; thus one of skill in the art would not be able to determine the limitations of the claimed method. Similarly, applicant has not defined the limitations of the "receptor activating dose" of claim 2 or the "vascular permeability modulating amount" of claim

7. Further, ORFV2-VEGF and NZ10 are laboratory designations that do not definitely identify the encompassed polypeptides. The definition on p. 13 does not clarify the meaning of these terms since it includes fragments, analogues and other variants, which are not defined so that one of skill in the art would recognize the metes and bounds of the invention. The polypeptides

should be referred to by reference to the identification number of an entered sequence rather than by an arbitrary designation.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lyttle et al. (J. Virol. Vol. 68, pp. 84-92, 1994) in view of Thomas (J. Biol. Chem. Vol. 271, pp. 603-606, 1996). Lyttle et al. teaches ORFV2-VEGF as a VEGF homologue and teaches that supernatants from cells infected with the OV NZ2 virus are mitogenic for vascular endothelial cells (p. 91). Lyttle et al. however fails to explicitly teach the use of ORFV2-VEGF to stimulate proliferation of endothelial cells or modulation of vascular permeability. Thomas teaches the use of mammalian VEGF to stimulate proliferation of endothelial cells (p. 605) through VEGF receptor-2 (KDR) (p. 604) and induce vascular permeability (p. 605) and teaches both *in vivo*

and *in vitro* effects (pp. 604-605). Thomas does not teach the use of ORFV2-VEGF for this purpose. However, it would have been obvious to one of ordinary skill in the art to combine the teachings of Lyttle et al. with those of Thomas to substitute ORFV2-VEGF in the method of Thomas to stimulate proliferation of endothelial cells and increase vascular permeability with a reasonable expectation of success because Thomas teaches that VEGF can be used to repair tissue injury (p. 605) and Lyttle et al. teaches ORFV2-VEGF as a VEGF homologue (p. 89) with similar mitogenic effects on endothelial cells (p.91).

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 305-3014 or (703) 308-4242.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly

Art Unit: 1646

signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.

October 10, 2000

Yvonne Eyer
YVONNE EYLER, PH.D
PRIMARY EXAMINER